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08/746361

APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO.
08/746,361	11/08/96	ANDERSON	D 012712-256

EXAMINER	
GAMBEL, P.	
ART UNIT	**PAPER NUMBER**
1806	7

18M1/0411

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DATE MAILED: 04/11/97

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☑ Responsive to communication(s) filed on _____

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s) or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☑ Claim(s) 1-28 is/are pending in the application.
Of the above, claim(s) 16-25, 27-28 is/are withdrawn from consideration.
☐ Claim(s) _____ is/are allowed.
☑ Claim(s) 1-3, 6, 7, 9-14 is/are rejected.
☐ Claim(s) _____ is/are objected to.
☑ Claim(s) 1-28 were subject to restriction or election requirement.

Application Papers

☑ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
☐ The specification is objected to by the Examiner.
☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.
☐ received in Application No. (Series Code/Serial Number) _____.
☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☑ Notice of Reference Cited, PTO-892
☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____
☐ Interview Summary, PTO-413
☑ Notice of Draftperson's Patent Drawing Review, PTO-948
☐ Notice of Informal Patent Application, PTO-152

–SEE OFFICE ACTION ON THE FOLLOWING PAGES–

DETAILED ACTION

1.The Art Unit location and the examiner of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1806.

2. Restriction to one of the following inventions is required under 35 U.S.C. § 121:

I. Claims 1-15 and 26, drawn to B7.1/B7.2-specific antibodies and compositions thereof, classified in Class 530, subclass 387.1 and Class 424, subclass, 130.1.,

II. Claims 16-25, 27-28, drawn to treating diseases with B7.1/B7.2-specific antibodies, classified in Class 424, subclass

3. Inventions I and II are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (M.P.E.P. § 806.05(h)). In the instant case, the antibodies as claimed can be used in a materially different process such as immunopurification procedures or diagnostic assays (or detection assays).

4. Because these inventions are distinct for the reasons given above and the search required for Group I is not required for Group II and Groups I and II have acquired a separate status in the art as shown by their different classification and divergent subject matter, restriction for examination purposes as indicated is proper.

5. This application contains claims directed to the following patentably distinct species of the claimed inventions I and II: wherein the antibody specificity is:

A) B7.1 or
B) B7.2.

These species are distinct because their structures and modes of action are different and their targeted molecules also differ in structure and mode of action.

Applicant is required under 35 U.S.C. § 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claim 1 (Invention I) and claims 16/17 (Invention II) are generic.

6. In addition, if Invention II is elected, the following election is required as it would apply to either the election of the B7.1-/ B7.2 specificity.

This application contains claims directed to the following patentably distinct species of the claimed invention II and the specificity of B7.1 or B7.2: wherein the disease is:

A) thrombocytopenia,
B) lupus,
C) diabetes,
D) arthritis,
E) psoriasis
F) anemia,
G) IBD,
H) allergy,
I) multiple sclerosis,
J) GVHD,
K) B cell lymphoma,
L) infectious diseases,
M) inflammatory diseases, or
N) autoimmunity.

These species are distinct because the pathological conditions differ in etiologies and therapeutic endpoints.

Applicant is required under 35 U.S.C. § 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claims 16 and 17 (Invention II) are generic to either the B7.1 and B7.2 specificity.

7. Applicant is advised that a response to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 C.F.R. § 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. M.P.E.P. § 809.02(a).

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. § 103 of the other invention.

8. Applicant is advised that the response to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed.

9. During a telephone conversation with Robin Teskin on 4/7/97, a provisional election was made with traverse to prosecute the invention of I, claims 1-15 and to select the species, B7.1-specific antibodies. Affirmation of this election must be made by applicant in responding to this Office action. Claims 16-28, drawn to Invention II and Invention I (including claims 4, 5, 8, 15), drawn to the specific B7.2-specific antibodies are withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b), as being drawn to a non-elected invention.

10. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 C.F.R. § 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a diligently-filed petition under 37 C.F.R. § 1.48(b) and by the fee required under 37 C.F.R. § 1.17(h).

11. Formal drawings and photographs have been submitted which fail to comply with 37 CFR 1.84. Please see the enclosed form PTO-948.

12. The application is required to be reviewed and all spelling, TRADEMARKS, and like errors corrected.

For example, the use of the trademark "SEPHAROSE" has been noted in this application. It should be capitalized or accompanied by the ™ or ® symbol wherever it appears and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the trademarks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Appropriate corrections are required.

13. The following is a quotation of the first paragraph of 35 U.S.C. § 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

14. The specification is objected to and claim 11 are rejected under 35 U.S.C. § 112, first paragraph, as failing to provide an adequate written description of the invention and failing to provide an enabling disclosure, because the specification does not provide evidence that the claimed biological materials are (1) known and readily available to the public; (2) reproducible from a written description (e.g. sequenced); or (3) deposited.

It unclear if a cell line which produces an antibody having the exact structural and chemical identity of 16C10, or 7C10 are known and publicly available, or can be reproducibly isolated without undue experimentation. Therefore, a suitable deposit for patent purposes is suggested. Without a publicly available deposit of the above cell line, one of ordinary skill in the art could not be assured of the ability to practice the invention as claimed. Exact replication of: (1) the claimed cell line; (2) a cell line which produces the chemically and functionally distinct antibody claimed; and/or (3) the

claimed antibody's amino acid or nucleic acid sequence is an unpredictable event.

For example, very different V_H chains (about 50% homologous) can combine with the same V_K chain to produce antibody-binding sites with nearly the same size, shape, antigen specificity, and affinity. A similar phenomenon can also occur when different V_H sequences combine with different V_K sequences to produce antibodies with very similar properties. The results indicate that divergent variable region sequences, both in and out of the complementarity-determining regions, can be folded to form similar binding site contours, which result in similar immunochemical characteristics. [FUNDAMENTAL IMMUNOLOGY 242 (William E. Paul, M.D. ed., 3d ed. 1993)]. Therefore, it would require undue experimentation to reproduce the claimed antibody species 16C10 and 7C10. Deposit of the appropriate hybridomas would satisfy the enablement requirements of 35 U.S.C. § 112, first paragraph. See, 37 C.F.R. 1.801-1.809.

In addition to the conditions under the Budapest Treaty, applicant is required to satisfy that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent in U.S. patent applications.

Amendment of the specification to recite the date of deposit and the complete name and address of the depository is required. As an additional means for completing the record, applicant may submit a copy of the contract with the depository for deposit and maintenance of each deposit.

If the original deposit is made after the effective filing date of an application for patent, the applicant should promptly submit a verified statement from a person in a position to corroborate the fact, and should state, that the biological material which is deposited is a biological material specifically identified in the application as filed, except if the person is an attorney or agent registered to practice before the Office, in which the case the statement need not be verified. See MPEP 1.804(b).

The sequence of an entire immunoglobulin satisfies the biological deposit of said immunoglobulin. Note that satisfaction for the biological deposit of the specific 16C10 and 7C10 antibodies require the disclosure and recitation of their entire amino acid sequence and not based upon partial sequences.

15. Claims 11 and 26 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claim 11 is indefinite in the recitation of "16C10" and "7C10" because their characteristics are not known. The use of "16C10" and "7C10" monoclonal antibodies as the sole means of identifying the claimed antibodies renders the claim indefinite because thee terms are merely laboratory designations which do not clearly define the claimed products, since different laboratories may use the same laboratory designations to define completely distinct cell lines or hybridomas.

B) Claim 26 is indefinite and ambiguous in the recitation of "suitable for treatment of a disease" since no disease or therapeutic endpoint is recited.

C) The amendments must be supported by the specification so as not to add any new matter.

16. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

17. The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

18. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 C.F.R. § 102(f) or (g) prior art under 35 C.F.R. § 103.

19. Claims 1-3, 6-7, 9 and 14 are rejected under 35 U.S.C. § 102(b) as being anticipated by Linsley et al. (PNAS, 1990) (see entire document). Linsley et al. teaches inhibitory B7-specific antibodies, including the BB-1 antibody. Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations addressed by the applicant would be inherent properties of the referenced antibodies. For example, the antibodies were used at 10 ug/ml. It is noted that the current designation of B7.1 refers to B7 as taught by this reference.

20. Claims 1-3, 6-7, 9 and 14 are rejected under 35 U.S.C. § 102(b) as being anticipated by Linsley et al. (J. Exp. Med., 1991) (see entire document). Linsely et al. teaches inhibitory B7-specific antibodies, including the BB-1 antibody. Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations addressed by the applicant would be inherent properties of the referenced antibodies. For example, the antibodies were used at 10 ug/ml.
It is noted that the current designation of B7.1 refers to B7 as taught by this reference.

21. Claims 1-3, 6-7, 9 and 14 are rejected under 35 U.S.C. § 102(b) as being anticipated by Linsley et al. (U.S. Patent No. 5,434,131) (see entire document). Linsely et al. teaches inhibitory B7-specific antibodies, including the BB-1 antibody, B7-specific antibodies that inhibit via CD28 and their use as pharmaceutical compositions. Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations addressed by the applicant would be inherent properties of the referenced antibodies. It is noted that the current designation of B7.1 refers to B7 as taught by this reference.

22. Claims 1-3, 6-7, 9 and 14 are rejected under 35 U.S.C. § 102(b) as being anticipated by Linsley et al. (U.S. Patent No. 5,521,288) (see entire document). Linsely et al. teaches inhibitory B7-specific antibodies, including the BB-1 antibody, B7-specific antibodies that inhibit via CD28 and their use as pharmaceutical compositions. Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations addressed by the applicant would be inherent properties of the referenced antibodies. It is noted that the current designation of B7.1 refers to B7 as taught by this reference.

23. Claims 1-3, 6-7, 9-14 are rejected under 35 U.S.C. § 103 as being unpatentable over Linsley et al. (PNAS, 1990), Linsley et al. (J. Exp. Med., 1991), Linsley et al. (U.S. Patent No. 5,434,131) or Linsley et al. (U.S. Patent No. 5,521,288) in view of art-known procedures and motivation to generate recombinant antibodies (e.g. humanized, chimeric or primatized) for diagnostic and therapeutic regimens as acknowledged on pages 15-20 and 24-27of the specification (e.g. Newman et al. Biotechnology, 1992).

Linsley et al. (PNAS), Linsley et al. (J. Exp. Med.) or Linsley et al. ('131) or Linsley et al. ('288) all teach the important role of CD28:B7 interactions in regulating immune responses, inhibiting said immune responses with B7-specific antibodies. These references differ from the claimed inventions by not explicitly reciting the instant 16C10 or 7C10 specificities and not teaching recombinant modifications of said B7-specific antibodies.

In agreement with the specification, it was well known in the art at the time the invention was made to chimerize/primatize/humanize antibodies to have readily available reagents suitable for human diagnosis and therapy and their respective use in primate models. For example, Newman et al. teach the protocols of primatizing antibodies including the use of computer analysis of the instant invention (see entire document). Although the references are silent about the exact sequences of the claimed 16C10 or 7C10-specific antibodies, the recombinant techniques and computer analyses of immunoglobulin sequences as taught by the references would have resulted in the same or very nearly the same characteristics of the instant claims since both the references and instant invention use the

same techniques, the same antibody specificities and the same goals. The generation of various forms of said antibodies would have resulted in both depleting and non-depleting antibodies, each with its own suitability based upon the needs of the targeted patient population or diagnostic assay. The ordinary artisan would have achieved either the same or functional equivalents of the instant 16C10, and 7C10 B7.1-specific antibodies. Also, note that the claims do not require that one generates the exact same antibody as 7C10 and 16C10, but rather isolates an antibody that has the same functional characteristics as said antibodies. Also, it is noted that the primary references and in particular the U.S. Patents are not restricted to the BB-1 antibody alone, but rather teach inhibitory B7-specific antibodies that inhibits interactions with CD28-positive T cell with B7 positive cells ('131: see column 13, paragraph 5; '756: see column 11, paragraph 5). The claimed functional limitations are expected properties of the B7-specific inhibitory antibodies. It is noted that the current designation of B7.1 refers to B7 as taught by these references.

One of ordinary skill in the art at the time the invention was made would have been motivated to select B7.1-specific antibodies thereof as diagnostic and therapeutic agents in treating human immunoregulatory disorders. From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

24. No claim is allowed.

25. Papers related to this application may be submitted to Group 1800 by facsimile transmission. Papers should be faxed to Group 1800 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 308-4242 or (703) 305-7939.

26. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (703) 308-3997. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lila Feisee can be reached on (703) 308-2731. Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1800 receptionist whose telephone number is (703) 308-0196.

Phillip Gambel, Ph.D.
Patent Examiner
Group 1800
April 8, 1997